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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,996	05/24/2000	Mark T. Keating	408-916010US	4041

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EXAMINER
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ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/554,996	Applicant(s) Keating et al.
	Examiner Shin-Lin Chen	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 18, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above, claim(s) *5, 15-21, 25, and 40-47* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6-14, 22-24, 26-39, and 48-59* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment filed 11-18-02 has been entered. Claims 1, 3, 6-9, 12-14, 22, 23, 26, 27, 30. 31 and 36-39 have been amended. Claims 48-59 have been added. Claims 1-59 are pending and claims 1-4, 6-14, 22-24, 26-39 and 48-59 are under consideration.

1. This application contains claims 5, 15-21, 25 and 40-47 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 6, 7, 10-14, 22-24, 26, 28-39, 48 and 50-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 11-18-02 necessitates this new ground of rejection.

The phrase "said elastin-based composition comprising a polypeptide having an amino acid sequence at least 80% identical to SEQ ID No. 2, SEQ ID No. 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1" in the amended claim 1 is vague and renders the claim indefinite. The metes and bounds of the claimed amino acid sequence is unclear. It is unclear whether the amino acid sequence is at least 80% identical

to SEQ ID No. 2 only or the amino acid sequence could also be either at least 80% identical to SEQ ID No. 3 or at least 80% identical to the peptide fragment of SEQ ID No. 2 or 3. It is also unclear whether only the peptide fragment thereof includes at least one hexameric sequence represented by SEQ ID No. 1 or the amino acid that is at least 80% identical to SEQ ID No. 2 or 3 would also contain at least one hexameric sequence represented by SEQ ID No. 1. Claims 2-4, 6, 7, 10-14, 22-24, 26, 28-39, 48 and 50-59 depend on claim 1 but fail to clarify the indefiniteness.

Similarly, the phrase "said elastin-based composition comprises a polypeptide having an amino acid sequence at least 90% identical to SEQ ID No. 2, SEQ ID No. 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1" in the newly added claim 48 is vague and renders the claim indefinite for the same reason as set forth above.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 6, 7, 10-14, 22-24, 26, 28-39, 48 and 50-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. Applicants' amendment filed 11-18-02 necessitates this new ground of rejection.

The phrase "said elastin-based composition comprising a polypeptide having an amino acid sequence at least 80% identical to SEQ ID No. 2, SEQ ID No. 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1" in the amended claim 1 is considered new matter. The specification states "preferred elastin-based compositions typically include elastin polypeptides having amino acid sequences that share at least 80%, preferably at least 90%, and most preferably at least 95% sequence identity with a native tropoelastin (specification, page 18, lines 7-9). The sequences of SEQ ID Nos. 1 and 2 are synthetic sequences. The specification fails to provide sufficient description for a elastin-based composition comprising a polypeptide having an amino acid sequence at least 80% identical to SEQ ID No. 2, or at least 80% identical to a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1.

Similarly, the phrase "said elastin-based composition comprises a polypeptide having an amino acid sequence at least 90% identical to SEQ ID No. 2, SEQ ID No. 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1" in the newly added claim 48 is considered new matter for the same reason as set forth above. Claims 2-4, 6, 7, 10-14, 22-24, 26, 28-39, 48 and 50-59 depend on claim 1. Thus, claims 1-4, 6, 7, 10-14, 22-24, 26, 28-39, 48 and 50-59 are rejected under 35 U.S.C. 112 first paragraph because the amended claims raise new matter issue.

The target site "trachea" recited in the amended claim 39 and newly added claim 53 is considered new matter. The specification fails to provide sufficient description for delivering the claimed pharmaceutical composition to trachea. The amendment filed 11-18-02 also fails to point out where in the specification has the support for delivering the claimed pharmaceutical composition to trachea.

6. Claims 1-4, 6-14, 22-24 and 26-39 remain rejected and claims 48-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a tropoelastin or 7 repeats of the sequence of SEQ ID No. 1 (VGVAPG) or a method for preventing vascular restenosis by using said composition *in vitro* or via direct administration of said composition to a targeted site *in vivo*, does not reasonably provide enablement for a pharmaceutical composition comprising a polypeptide having an amino acid sequence at least 80% or 90% identical to SEQ ID No. 2, SEQ ID No. 3, or a peptide fragment thereof including at least one hexameric sequence represented by SEQ ID No. 1 and a method for prophylaxis or treatment of a disorder having diminished capacity to regulate smooth muscle cell function, including vascular stenosis, obstructive vascular disease, stenosis and restenosis, by delivering said pharmaceutical composition to a targeted site via any administration route *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 5-10-02 (Paper No. 8).

Applicants argue that the specification is broadly enabling for pharmaceutical preparation of elastin-based composition for administration to target sites in vivo and the claims have been amended to describe structural attributes and functional attributes (amendment, p. 12). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-10-02 (Paper No. 8) and that the amendment filed 11-18-02 of claims 1 and 48 render the claims indefinite as discussed above under 35 U.S.C. 112 second paragraph rejection. In addition, a polypeptide having amino acid sequence at least 80% or 90% identical to SEQ ID No. 2 or 3 encompasses numerous unknown and unidentified polypeptide sequences having amino acid sequence added at 3', 5' and/or within the sequence of SEQ ID No. 2 or 3. As discussed in the preceding Official action mailed 5-10-02 (Paper No. 8), different elastin or tropoelastin derived from different organisms can have different types of repeat that might contribute to the biological function of elastin or tropoelastin. It was unclear at the time of the invention whether the VGVAPG repeat and how many VGVAPG repeat is the structural feature required for the biological activity of elastin or tropoelastin. Further, it was well known in the art that amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Polypeptide function was unpredictable from mere amino acid sequence at the time of the invention. Thus, it would

require one skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed.

Applicants argue that the claims are limited to compositions having particular functional attributes capable of evoking a particular response upon administration and the composition that do not evoke said response would lie beyond the scope of the claimed subject matter. Applicants further argue that "the presence of inoperative embodiment within the scope of a claim does not necessarily render a claim nonenabled" (amendment, p. 12-13). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-10-02 (Paper No. 8) and the reasons set forth above. The amended claims still read on administration of a pharmaceutical composition to a targeted site via various administration routes. The claims broadly encompass a pharmaceutical composition comprising numerous unknown and unidentified polypeptide sequences having amino acid sequence added at 3', 5' and/or within the sequence of SEQ ID No. 2 or 3, or peptide fragment thereof and a method for prophylaxis or treatment of a disorder having diminished capacity to regulate smooth muscle cell function, including vascular stenosis, obstructive vascular disease, stenosis and restenosis, by delivering said pharmaceutical composition to a targeted site via various administration routes *in vivo*. It was known in the art that administration route of a pharmaceutical composition plays an important role in the efficiency of said composition *in vivo*. The type of administration route determines how the pharmaceutical composition reach its targeted site *in vivo*. The location of administration, the amount and stability of the polypeptides or peptides *in vivo*, and its compartmentalization within

the cell are all important factors in determining whether sufficient polypeptides or peptides can reach their target site so as to provide therapeutic effects for preventing or treating disorders *in vivo*. Although "the presence of inoperative embodiment within the scope of a claim does not necessarily render a claim nonenabled", the specification must provide sufficient enabling disclosure for the full scope of the invention claimed. However, the specification fails to do so, thus, one skilled in the art at the time of the invention would require to engage in undue experimentation to practice over the full scope of the invention claimed in view of the reasons set forth in the preceding Official action mailed 5-10-02 (Paper No. 8) and the reasons set forth above.

Conclusion

No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MEP. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.